

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: :
Bernd RIEDL et al. : Group Art Unit: TO BE ASSIGNED
Serial No.: TO BE ASSIGNED : Examiner: TO BE ASSIGNED
Filed: January 11, 2002 :
For: ω -CARBOXYARL SUBSTITUTED DIPHENYL UREAS AS RAF KINASE
INHIBITORS

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to the calculation of the fee for the examination of the accompanying application,
please amend the claims as follows.

IN THE SPECIFICATION

Page 1, line 1, after the title insert

--Priority is claimed to provisional application Serial No. (Unassigned), filed on January
12, 2001.--

IN THE CLAIMS

Please cancel claims 4, 5, 14, 16, 20, 23-26, 29-31, 34-36, 40-43, 51 and 55-65 without
prejudice or disclaimer.

Please amend claims 1-3, 6-13, 15, 17-19, 21, 27, 28, 32, 33, 37-39, 44-50 and 52-54 as
follows.

1. (Amended) A method for the treatment of cancerous cell growth mediated by RAF

kinase, comprising administering a compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is $-\text{NH}-\text{C}(\text{O})-\text{NH}-$,

A is a substituted moiety of up to 40 carbon atoms of the formula: $-\text{L}-(\text{M}-\text{L}^1)_q$, where L is a 5 or 6 membered cyclic structure bound directly to D, L^1 comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and L^1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur,

wherein L^1 is substituted by at least one substituent selected from the group consisting of $-\text{SO}_2\text{R}_x$, $-\text{C}(\text{O})\text{R}_x$ and $-\text{C}(\text{NR}_y)\text{R}_z$,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo,

R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms

selected from N, S and O and are optionally substituted by halogen, or

$-\text{OSi}(\text{R}_f)_3$ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_a or R_b is $-\text{C}(\text{O})-$, a C_1 - C_5 divalent alkylene group or a substituted C_1 - C_5 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1 - C_5 divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L^1 is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and W_n , where n is 0-3;

wherein each W is independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^7$, $-\text{C}(\text{O})\text{NR}^7\text{R}^7$, $-\text{C}(\text{O})-\text{R}^7$, $-\text{NO}_2$, $-\text{OR}^7$, $-\text{SR}^7$, $-\text{NR}^7\text{R}^7$, $-\text{NR}^7\text{C}(\text{O})\text{OR}^7$, $-\text{NR}^7\text{C}(\text{O})\text{R}^7$, $-\text{Q}-\text{Ar}$, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^7$, $-\text{C}(\text{O})\text{R}^7$, $-\text{C}(\text{O})\text{NR}^7\text{R}^7$, $-\text{OR}^7$, $-\text{SR}^7$, $-\text{NR}^7\text{R}^7$, $-\text{NO}_2$, $-\text{NR}^7\text{C}(\text{O})\text{R}^7$, $-\text{NR}^7\text{C}(\text{O})\text{OR}^7$ and halogen up to per-halo; with each R^7 independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is $-\text{O}-$, $-\text{S}-$, $-\text{N}(\text{R}^7)-$, $-(\text{CH}_2)_m-$, $-\text{C}(\text{O})-$, $-\text{CH}(\text{OH})-$, $-(\text{CH}_2)_m\text{O}-$, $-(\text{CH}_2)_m\text{S}-$,

$-(CH_2)_mN(R^7)-$, $-O(CH_2)_m-CHX^a-$, $-CX^a_2-$, $-S-(CH_2)_m-$ and $-N(R^7)(CH_2)_m-$, where $m=1-3$, and X^a is halogen; and

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1} , wherein $n1$ is 0 to 3 and each Z is independently selected from the group consisting of $-CN$, $-CO_2R^7$, $-C(O)R^7$, $-C(O)NR^7R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of $-CN$, $-CO_2R^7$, $-COR^7$, $-C(O)NR^7R^7$, $-OR^7$, $-SR^7$, $-NO_2$, $-NR^7R^7$, $-NR^7C(O)R^7$, and $-NR^7C(O)OR^7$, with R^7 as defined above.

2. (Amended) A method as in claim 1 wherein:

R_y is hydrogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{3-10} cycloalkyl having 0-3 heteroatoms, C_{2-10} alkenyl, C_{1-10} alkenoyl, C_{6-12} aryl, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{7-24} aralkyl, C_{7-24} alkaryl, substituted C_{1-10} alkyl, substituted C_{1-10} alkoxy, substituted C_{3-10} cycloalkyl having 0-3 heteroatoms selected from N, S and O, substituted C_6-C_{14} aryl, substituted C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, substituted C_{7-24} alkaryl or substituted C_7-C_{24} aralkyl, where R_y is a substituted group, it is substituted by halogen up to per halo,

R_z is hydrogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{3-10} cycloalkyl having 0-3 heteroatom, C_{2-10} alkenyl, C_{1-10} alkenoyl, C_{6-12} aryl, C_3-C_{12} hetaryl having 1-3 heteroatoms selected from, S, N and O, C_{7-24} alkaryl, C_{7-24} aralkyl, substituted C_{1-10} alkyl, substituted C_{1-10} alkoxy, substituted C_6-C_{14} aryl, substituted C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from S, N and O, substituted C_{3-12} hetaryl having 1-3 heteroatoms selected from S, N and O, substituted C_{7-24} alkaryl or substituted C_7-C_{24} aralkyl where R_z is a substituted group, it is substituted by halogen up to per halo, hydroxy, C_{1-10} alkyl, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{1-10} alkoxy, C_{6-12} aryl, C_{1-6} halo substituted alkyl up to per halo alkyl, C_6-C_{12} halo substituted aryl up to per halo aryl, C_3-C_{12} halo

substituted cycloalkyl up to per halo cycloalkyl having 0-3 heteroatoms selected from N, S and O, halo substituted C₃-C₁₂ hetaryl up to per halo hetaryl having 1-3 heteroatoms selected from O, N and S, halo substituted C₇-C₂₄ aralkyl up to per halo aralkyl, halo substituted C₇-C₂₄ alkaryl up to per halo alkaryl, and -C(O)R_g,

R_a and R_b are,

a) independently hydrogen,

a carbon based moiety selected from the group consisting of C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₃₋₁₀ cycloalkyl, C₂₋₁₀ alkenyl, C₁₋₁₀ alkenoyl, C₆₋₁₂ aryl, C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from O, N and S, C₃₋₁₂ cycloalkyl having 0-3 heteroatoms selected from N, S and O, C₇₋₂₄ aralkyl, C₇-C₂₄ alkaryl, substituted C₁₋₁₀ alkyl, substituted C₁₋₁₀ alkoxy, substituted C₃₋₁₀ cycloalkyl, having 0-3 heteroatoms selected from N, S and O, substituted C₆₋₁₂ aryl, substituted C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from N, S and O, substituted C₇₋₂₄ aralkyl, substituted C₇₋₂₄ alkaryl, where R_a and R_b are a substituted group, they are substituted by halogen up to per halo, hydroxy, C₁₋₁₀ alkyl, C₃₋₁₂ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from N, S and O, C₁₋₁₀ alkoxy, C₆₋₁₂ aryl, C₁₋₆ halo substituted alkyl up to per halo alkyl, C₆-C₁₂ halo substituted aryl up to per halo aryl, C₃-C₁₂ halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C₃-C₁₂ hetaryl up to per halo heteraryl, halo substituted C₇-C₂₄ aralkyl up to per halo aralkyl, halo substituted C₇-C₂₄ alkaryl up to per halo alkaryl, and -C(O)R_g; or

-OSi(R_f)₃ where R_f is hydrogen, C₁₋₁₀ alkyl, C₁₋₁₀ alkoxy, C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₆₋₁₂ aryl, C₃-C₁₂ hetaryl having 1-3 heteroatoms selected from O, S and N, C₇₋₂₄ aralkyl, substituted C₁₋₁₀ alkyl, substituted C₁-C₁₀ alkoxy, substituted C₃-C₁₂ cycloalkyl having 0-3 heteroatoms selected from O, S and N, substituted C₃-C₁₂ heteraryl having 1-3 heteroatoms selected from O, S, and N, substituted C₆₋₁₂ aryl, and substituted C₇₋₂₄ alkaryl, where R_f is a substituted group it is substituted halogen up to per halo, hydroxy, C₁₋₁₀ alkyl, C₃₋₁₂ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₃₋₁₂

hetaryl having 1-3 heteroatoms selected from N, S and O, C₁₋₁₀ alkoxy, C₆₋₁₂ aryl, C_{7-C₂₄} alkaryl, C_{7-C₂₄} aralkyl, C₁₋₆ halo substituted alkyl up to per halo alkyl, C_{6-C₁₂} halo substituted aryl up to per halo aryl, C_{3-C₁₂} halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C_{3-C₁₂} hetaryl up to per halo heteraryl, halo substituted C_{7-C₂₄} aralkyl up to per halo aralkyl, halo substituted C_{7-C₂₄} alkaryl up to per halo alkaryl, and -C(O)R_g,

or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O with substituents selected from the group consisting of halogen up to per halo, hydroxy, C₁₋₁₀ alkyl, C₃₋₁₂ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from N, S and O, C₁₋₁₀ alkoxy, C₆₋₁₂ aryl, C_{7-C₂₄} alkaryl, C_{7-C₂₄} aralkyl, halo substituted C₁₋₆ alkyl up to per halo alkyl, halo substituted C_{6-C₁₂} aryl up to per halo aryl, halo substituted C_{3-C₁₂} cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C_{3-C₁₂} hetaryl up to per halo heteraryl, halo substituted C_{7-C₂₄} aralkyl up to per halo aralkyl, halo substituted C_{7-C₂₄} alkaryl up to per halo alkaryl, and -C(O)R_g,

or

c) one of R_a or R_b is -C(O)-, a C_{1-C₅} divalent alkylene group or a substituted C_{1-C₅} divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_{1-C₅} divalent alkylene group are selected from the group consisting of halogen, hydroxy, C₁₋₁₀ alkyl, C₃₋₁₂ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from N, S and O, C₁₋₁₀ alkoxy, C₆₋₁₂ aryl, C_{7-C₂₄} alkaryl, C_{7-C₂₄} aralkyl, C₁₋₆ halo substituted alkyl up to per halo alkyl, C_{6-C₁₂} halo substituted aryl up to per halo aryl, C_{3-C₁₂} halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C_{3-C₁₂} hetaryl up to per halo heteraryl, halo substituted C_{7-C₂₄} aralkyl up to per halo aralkyl, halo substituted C_{7-C₂₄} alkaryl up to per halo alkaryl, and -C(O)R_g,

where R_g is C_{1-10} alkyl; $-CN$, $-CO_2R_d$, $-OR_d$, $-SR_d$, $-NO_2$, $-C(O)R_e$, $-NR_dR_e$, $-NR_dC(O)OR_e$ and $-NR_dC(O)R_e$, and R_d and R_e are independently selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{3-10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, C_{6-12} aryl, C_3-C_{12} hetaryl with 1-3 heteroatoms selected from O, N and S and C_7-C_{24} aralkyl, C_7-C_{24} alkaryl, up to per halo substituted C_1-C_{10} alkyl, up to per halo substituted C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, up to per halo substituted C_6-C_{14} aryl, up to per halo substituted C_3-C_{12} hetaryl having 1-3 heteroatoms selected from O, N, and S, halo substituted C_7-C_{24} alkaryl up to per halo alkaryl, and up to per halo substituted C_7-C_{24} aralkyl,

W is independently selected from the group consisting of $-CN$, $-CO_2R^7$, $-C(O)NR^7R^7$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, C_2-C_{10} alkenyl, C_1-C_{10} alkenoyl, C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_6-C_{14} aryl, C_7-C_{24} alkaryl, C_7-C_{24} aralkyl, C_3-C_{12} heteroaryl having 1-3 heteroatoms selected from O, N and S, C_4-C_{23} alkheteroaryl having 1-3 heteroatoms selected from O, N and S, substituted C_1-C_{10} alkyl, substituted C_1-C_{10} alkoxy, substituted C_2-C_{10} alkenyl, substituted C_1-C_{10} alkenoyl, substituted C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, substituted C_6-C_{12} aryl, substituted C_3-C_{12} hetaryl having 1-3 heteroatoms selected from O, N and S, substituted C_7-C_{24} aralkyl, substituted C_7-C_{24} alkaryl, substituted C_4-C_{23} alkheteroaryl having 1-3 heteroatoms selected from O, N and S, and $-Q-Ar$;

R^7 is independently selected from H, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, C_2-C_{10} alkenyl, C_1-C_{10} alkenoyl, C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_6-C_{14} aryl, C_3-C_{13} hetaryl having 1-3 heteroatoms selected from O, N and S, C_7-C_{14} alkaryl, C_7-C_{24} aralkyl, C_4-C_{23} alkheteroaryl having 1-3 heteroatoms selected from O, N and S, up to per-halosubstituted C_1-C_{10} alkyl, up to per-halosubstituted C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, up to per-halosubstituted C_6-C_{14} aryl, up to per-halosubstituted C_3-C_{13} hetaryl having 1-3 heteroatoms selected from O, N and S, up to per-halosubstituted C_7-C_{24} aralkyl, up to per-

halosubstituted C₇-C₂₄ alkaryl, and up to per-halosubstituted C₄-C₂₃ alkheteroaryl; and

each Z is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₂-C₁₀ alkenyl, C₁-C₁₀ alkenoyl, C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, N and S, C₆-C₁₄ aryl, C₃-C₁₃ hetaryl having 1-3 heteroatoms selected from O, N and S, C₇-C₂₄ alkaryl, C₇-C₂₄ aralkyl, C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S, substituted C₁-C₁₀ alkyl, substituted C₁-C₁₀ alkoxy, substituted C₂-C₁₀ alkenyl, substituted C₁-C₁₀ alkenoyl, substituted C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, N and S, substituted C₆-C₁₂ aryl, substituted C₇-C₂₄ alkaryl, substituted C₇-C₂₄ aralkyl and substituted C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S; wherein if Z is a substituted group, the one or more substituents are selected from the group consisting of -CN, -CO₂R⁷, -COR⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NO₂, -NR⁷R⁷, -NR⁷C(O)R⁷, and -NR⁷C(O)OR⁷.

3. (Amended) A method as in claim 1 wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m-, CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, X^a is halogen and R⁷ is as defined in claim 1.

6. (Amended) A method of claim 1 wherein B of Formula I is an unsubstituted phenyl group, an unsubstituted pyridyl group, an unsubstituted pyrimidinyl, a phenyl group substituted by a substituent selected from the group consisting of halogen and W_n wherein W and n are as defined in claim 1, a pyrimidinyl group substituted by a substituent selected from the group consisting of halogen and W_n, whereas W and n are as defined in Claim 1, or a substituted pyridyl group substituted by a substituent selected from the group consisting of halogen and W_n wherein W and n are as defined in claim 1.

7. (Amended) A method of claim 6 wherein B of Formula I is a substituted phenyl group, a substituted pyrimidinyl group, or substituted pyridyl group substituted 1 to 3 times by 1 or more substituents selected from the group consisting of -CN, halogen, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, -OH, up to per halo substituted C₁-C₁₀ alkyl, up to per halo substituted C₁-C₁₀ alkoxy or

phenyl substituted by halogen up to per halo.

8. (Amended) A method of claim 1, wherein L, the six member cyclic structure bound directly to D, is a substituted or unsubstituted 6 member aryl moiety or a substituted or unsubstituted 6 member hetaryl moiety, wherein said hetaryl moiety has 1 to 4 members selected from the group of heteroatoms consisting of nitrogen, oxygen and sulfur with the balance of said hetaryl moiety being carbon, wherein the one or more substituents are selected from the group consisting of halogen and W_n wherein W and n are as defined in claim 1.

9. (Amended) A method of claim 8, wherein L, the 6 member cyclic structure bound directly to D, is a substituted phenyl, unsubstituted phenyl, substituted pyrimidinyl, unsubstituted pyrimidinyl, substituted pyridyl or unsubstituted pyridyl group.

10. (Amended) A method of claim 1, wherein said substituted cyclic moiety L¹ comprises a 5 to 6 membered aryl moiety or hetaryl moiety, wherein said heteraryl moiety comprises 1 to 4 members selected from the group of heteroatoms consisting of nitrogen, oxygen and sulfur.

11. (Amended) A method of claim 2, wherein said substituted cyclic moiety L¹ is phenyl, pyridinyl or pyrimidinyl.

12. (Amended) A method of claim 3, wherein said substituted cyclic moiety L¹ is phenyl, pyridinyl or pyrimidinyl.

13. (Amended) A method of claim 8, wherein said substituted cyclic moiety L¹ is phenyl, pyridinyl or pyrimidinyl.

15. (Amended) A method of claim 8, wherein said substituted cyclic moiety L¹ is phenyl, pyridinyl or pyrimidinyl.

17. (Amended) A method of claim 10, wherein said substituted cyclic moiety L¹ is phenyl, pyridinyl or pyrimidinyl.

18. (Amended) A method of claim 17, wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m- CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m=

1-3, X^a is halogen and R^7 is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.

19. (Amended) A method of claim 15, wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R^7)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R^7)-, -O(CH₂)_m-CHX^a-, -CX₂^a-, -S-(CH₂)_m- and -N(R^7)(CH₂)_m-, where m= 1-3, X^a is halogen and R^7 is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.

21. (Amended) A method of claim 17, wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R^7)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R^7)-, -O(CH₂)_m-CHX^a-, -CX₂^a-, -S-(CH₂)_m- and -N(R^7)(CH₂)_m-, where m= 1-3, X^a is halogen and R^7 is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.

27. (Amended) A method of claim 21 wherein L^1 is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C₁-C₁₀ alkyl, up to per halo substituted C₁-C₁₀ alkyl, -CN, -OH, halogen, C₁-C₁₀ alkoxy and up to per halo substituted C₁-C₁₀ alkoxy.

28. (Amended) A method of claim 1 wherein L^1 is substituted by -C(O) R_x .

32. (Amended) A method of claim 1 wherein L^1 is substituted by -C(O) R_x or -SO₂ R_x , wherein R_x is NR_aR_b.

33. (Amended) A method of claim 13 wherein L^1 is substituted by -C(O) R_x or -SO₂ R_x , wherein R_x is NR_aR_b, and R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

-OSi(R_f)₃ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_a or R_b is -C(O)-, a C₁-C₅ divalent alkylene group or a substituted C₁-C₅ divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C₁-C₅ divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.

37. (Amended) A method of claim 21 wherein L¹ is substituted by -C(O)R_x or -SO₂R_x, wherein R_x is NR_aR_b and R_a and R_b are independently hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.

38. (Amended) A method for the treatment of cancerous cell growth mediated by RAF kinase, comprising administering a compound of Formula I:

A - D - B

(I)

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH- ,

A is a substituted moiety of up to 40 carbon atoms of the formula: $\text{-L-(M-L}^1\text{)}_q$, where L is a 6 membered aryl moiety or a 6 membered hetaryl moiety bound directly to D, L^1 comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and L^1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur,

wherein L^1 is substituted by at least one substituent selected from the group consisting of $\text{-SO}_2\text{R}_x$, -C(O)R_x and $\text{-C(NR}_y\text{)R}_z$,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo,

R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

$\text{-OSi(R}_f\text{)}_3$ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by

halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_a or R_b is $-C(O)-$, a C_1-C_5 divalent alkylene group or a substituted C_1-C_5 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1-C_5 divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L^1 is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and W_n , where n is 0-3;

wherein each W is independently selected from the group consisting of $-CN$, $-CO_2R^7$, $-C(O)NR^7R^7$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, $-Q-Ar$, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of $-CN$, $-CO_2R^7$, $-C(O)R^7$, $-C(O)NR^7R^7$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NO_2$, $-NR^7C(O)R^7$, $-NR^7C(O)OR^7$ and halogen up to per-halo; with each R^7 independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is $-O-$, $-S-$, $-N(R^7)-$, $-(CH_2)_m-$, $-C(O)-$, $-CH(OH)-$, $-(CH_2)_mO-$, $-(CH_2)_mS-$, $-(CH_2)_mN(R^7)-$, $-O(CH_2)_m-$, $-CHX^a-$, $-CX^a_2-$, $-S-(CH_2)_m-$ and $-N(R^7)(CH_2)_m-$, where $m=1-3$, and X^a is halogen;

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to

per-halo, and optionally substituted by Z_{n1} , wherein $n1$ is 0 to 3 and each Z is independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^7$, $-\text{C}(\text{O})\text{R}^7$, $-\text{C}(\text{O})\text{NR}^7\text{R}^7$, $-\text{NO}_2$, $-\text{OR}^7$, $-\text{SR}^7$, $-\text{NR}^7\text{R}^7$, $-\text{NR}^7\text{C}(\text{O})\text{OR}^7$, $-\text{NR}^7\text{C}(\text{O})\text{R}^7$, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents are selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^7$, $-\text{COR}^7$, $-\text{C}(\text{O})\text{NR}^7\text{R}^7$, $-\text{OR}^7$, $-\text{SR}^7$, $-\text{NO}_2$, $-\text{NR}^7\text{R}^7$, $-\text{NR}^7\text{C}(\text{O})\text{R}^7$, and $-\text{NR}^7\text{C}(\text{O})\text{OR}^7$, with R^7 as defined above; and

wherein M is one or more bridging groups selected from the group consisting of $-\text{O}-$, $-\text{S}-$, $-\text{N}(\text{R}^7)-$, $-(\text{CH}_2)_m-$, $-\text{C}(\text{O})-$, $-\text{CH}(\text{OH})-$, $-(\text{CH}_2)_m\text{O}-$, $-(\text{CH}_2)_m\text{S}-$, $-(\text{CH}_2)_m\text{N}(\text{R}^7)-$, $-\text{O}(\text{CH}_2)_m-$, CHX^a- , $-\text{CX}^a_2-$, $-\text{S}-(\text{CH}_2)_m-$ and $-\text{N}(\text{R}^7)(\text{CH}_2)_m-$, where $m=1-3$, X^a is halogen.

39. (Amended) A method for the treatment of cancerous cell growth mediated by RAF kinase, comprising administering a compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is $-\text{NH}-\text{C}(\text{O})-\text{NH}-$,

A is a substituted moiety of up to 40 carbon atoms of the formula: $-\text{L}-(\text{M}-\text{L}^1)_q$, where L is a substituted or unsubstituted phenyl or pyridinyl moiety bound directly to D , L^1 comprises a substituted phenyl, pyridinyl or pyrimidinyl moiety, M is a bridging group having at least one atom, q is an integer of from 1-3; and

B is a substituted or unsubstituted phenyl or pyridine group bound directly to D ,

wherein L^1 is substituted by at least one substituent selected from the group consisting of $-\text{SO}_2\text{R}_x$, $-\text{C}(\text{O})\text{R}_x$ and $-\text{C}(\text{NR}_y)\text{R}_z$,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo, and ;

R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms

selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

$-OSi(R_f)_3$ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_a or R_b is $-C(O)-$, a C_1-C_5 divalent alkylene group or a substituted C_1-C_5 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1-C_5 divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L^1 is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and W_n , where n is 0-3;

wherein each W is independently selected from the group consisting of $-CN$, $-CO_2R^7$, $-C(O)NR^7R^7$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, $-Q-Ar$, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from

the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^7$, $-\text{C}(\text{O})\text{R}^7$, $-\text{C}(\text{O})\text{NR}^7\text{R}^7$, $-\text{OR}^7$, $-\text{SR}^7$, $-\text{NR}^7\text{R}^7$, $-\text{NO}_2$, $-\text{NR}^7\text{C}(\text{O})\text{R}^7$, $-\text{NR}^7\text{C}(\text{O})\text{OR}^7$ and halogen up to per-halo; with each R^7 independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is $-\text{O}-$, $-\text{S}-$, $-\text{N}(\text{R}^7)-$, $-(\text{CH}_2)_m-$, $-\text{C}(\text{O})-$, $-\text{CH}(\text{OH})-$, $-(\text{CH}_2)_m\text{O}-$, $-(\text{CH}_2)_m\text{S}-$, $-(\text{CH}_2)_m\text{N}(\text{R}^7)-$, $-\text{O}(\text{CH}_2)_m-\text{CHX}^a$, $-\text{CX}^a_2-$, $-\text{S}-(\text{CH}_2)_m-$ and $-\text{N}(\text{R}^7)(\text{CH}_2)_m-$, where $m = 1-3$, and X^a is halogen;

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1} , wherein $n1$ is 0 to 3 and each Z is independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^7$, $-\text{C}(\text{O})\text{R}^7$, $-\text{C}(\text{O})\text{NR}^7\text{R}^7$, $-\text{NO}_2$, $-\text{OR}^7$, $-\text{SR}^7$, $-\text{NR}^7\text{R}^7$, $-\text{NR}^7\text{C}(\text{O})\text{OR}^7$, $-\text{NR}^7\text{C}(\text{O})\text{R}^7$, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^7$, $-\text{COR}^7$, $-\text{C}(\text{O})\text{NR}^7\text{R}^7$, $-\text{OR}^7$, $-\text{SR}^7$, $-\text{NO}_2$, $-\text{NR}^7\text{R}^7$, $-\text{NR}^7\text{C}(\text{O})\text{R}^7$, and $-\text{NR}^7\text{C}(\text{O})\text{OR}^7$; and

wherein M is one or more bridging groups selected from the group consisting of $-\text{O}-$, $-\text{S}-$, $-\text{N}(\text{R}^7)-$, $-(\text{CH}_2)_m-$, $-\text{C}(\text{O})-$, $-\text{CH}(\text{OH})-$, $-(\text{CH}_2)_m\text{O}-$, $-(\text{CH}_2)_m\text{S}-$, $-(\text{CH}_2)_m\text{N}(\text{R}^7)-$, $-\text{O}(\text{CH}_2)_m-\text{CHX}^a$, $-\text{CX}^a_2-$, $-\text{S}-(\text{CH}_2)_m-$ and $-\text{N}(\text{R}^7)(\text{CH}_2)_m-$, where $m = 1-3$, X^a is halogen.

44. (Amended) A method as in claim 38 wherein substituents for B and L and additional substituents for L^1 , are selected from the group consisting of $\text{C}_1\text{-C}_{10}$ alkyl up to per halo substituted $\text{C}_1\text{-C}_{10}$ alkyl, CN, OH, halogen, $\text{C}_1\text{-C}_{10}$ alkoxy and up to per halo substituted $\text{C}_1\text{-C}_{10}$ alkoxy.

45. (Amended) A method as in claim 39 wherein substituents for B and L and additional substituents for L^1 , are selected from the group consisting of $\text{C}_1\text{-C}_{10}$ alkyl up to per halo substituted $\text{C}_1\text{-C}_{10}$ alkyl, CN, OH, halogen, $\text{C}_1\text{-C}_{10}$ alkoxy and up to per halo substituted $\text{C}_1\text{-C}_{10}$ alkoxy.

46. (Amended) A method of claim 38 wherein L^1 is substituted by $\text{C}(\text{O})\text{R}_x$ or SO_2R_x .

47. (Amended) A method of claim 39 wherein L^1 is substituted by $\text{C}(\text{O})\text{R}_x$ or SO_2R_x .

48. (Amended) A method of claim 46 wherein R_x is NR_aR_b and R_a and R_b are independently hydrogen and a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen..

49. (Amended) A method of claim 47 wherein R_x is NR_aR_b and R_a and R_b are independently hydrogen and a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.

50. (Amended) A method of claim 1 wherein the compound of formula 1 is a pharmaceutically acceptable salt selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

52. (Amended) A method of claim 33 wherein the compound of formula 1 is a pharmaceutically acceptable salt selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid,

maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

53. (Amended) A method of claim 38 wherein the compound formula 1 is a pharmaceutically acceptable salt selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

54. (Amended) A method of claim 39 wherein the compound of formula 1 is a pharmaceutically acceptable salt selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

Please add new claims 68-83 as follows.

--68. A method as in claim 1 for the treatment of solid cancers.

69. A method as in claim 1 for the treatment of carcinomas, myleoid disorders or adenomas.

70. A method as in claim 28 for the treatment of carcinomas, myleoid disorders or adenomas.

71. A method as in claim 39 for the treatment of carcinomas, myleoid disorders or adenomas.

72. A method as in claim 50 for the treatment of carcinomas, myleoid disorders or adenomas.

73. A method as in claim 67 for the treatment of carcinomas, myleoid disorders or adenomas.

74. A method as in claim 1 for the treatment of carcinoma of the lung, pancreas, thyroid, bladder or colon.

75. A method as in claim 28 for the treatment of carcinoma of the lung, pancreas, thyroid, bladder or colon.

76. A method as in claim 39 for the treatment of carcinoma of the lung, pancreas, thyroid, bladder or colon.

77. A method as in claim 50 for the treatment of carcinoma of the lung, pancreas, thyroid, bladder or colon.

78. A method as in claim 67 for the treatment of carcinoma of the lung, pancreas, thyroid, bladder or colon.

79. A method as in claim 1 for the treatment of myeloid leukemia or villous colon adenomas.

80. A method as in claim 28 for the treatment of myeloid leukemia or villous colon adenomas.

81. A method as in claim 39 for the treatment of myeloid leukemia or villous colon adenomas.

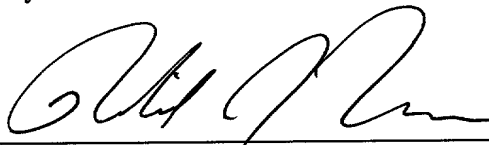
82. A method as in claim 50 for the treatment of myeloid leukemia or villous colon adenomas.

83. A method as in claim 67 for the treatment of myeloid leukemia or villous colon adenomas.--

REMARKS

Support for new claims 68-83 is found on page 2, lines 21-24, and page 11, line 9 - page 14, line 30.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

claims 4, 5, 14, 16, 20, 23-26, 29-31, 34-36, 40-43, 51 and 55-65 have been canceled.

Claims 1-3, 6-13, 15, 17-19, 21, 27, 28, 32, 33, 37-39, 44-50 and 52-54 have been amended as follows:

1. (Amended) A method for the treatment of cancerous cell growth mediated by RAF kinase, comprising administering a compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is $-NH-C(O)-NH-$,

A is a substituted moiety of up to 40 carbon atoms of the formula: $-L-(M-L^1)_q$, where L is a 5 or 6 membered cyclic structure bound directly to D, L^1 comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and L^1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur,

wherein L^1 is substituted by at least one substituent selected from the group consisting of $-SO_2R_x$, $-C(O)R_x$ and $-C(NR_y)R_z$,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo,

R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and

wherein each W is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)NR⁷R⁷, -C(O)-R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, -Q-Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NR⁷R⁷, -NO₂, -NR⁷C(O)R⁷, -NR⁷C(O)OR⁷ and halogen up to per-halo; with each R⁷ independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m-CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, and X^a is halogen; and

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of -CN, -CO₂R⁷, -COR⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NO₂, -NR⁷R⁷, -NR⁷C(O)R⁷, and -NR⁷C(O)OR⁷, with R⁷ as defined above.

2. (Amended) A method [compound] as in claim 1 wherein:

R_y is hydrogen, C₁₋₁₀ alkyl, C₁₋₁₀ alkoxy, C₃₋₁₀ cycloalkyl having 0-3 heteroatoms, C₂₋₁₀ alkenyl, C₁₋₁₀ alkenoyl, C₆₋₁₂ aryl, C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from N, S and O, C₇₋₂₄ aralkyl, C₇₋₂₄ alkaryl, substituted C₁₋₁₀ alkyl, substituted C₁₋₁₀ alkoxy, substituted C₃₋₁₀ cycloalkyl having 0-3 heteroatoms selected from N, S and O, substituted C₆-C₁₄ aryl, substituted C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from N, S and O, substituted C₇₋₂₄ alkaryl or substituted C₇-C₂₄ aralkyl, where R_y is a substituted group, it is substituted by halogen up to per halo,

R_z is hydrogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{3-10} cycloalkyl having 0-3 heteroatom, C_{2-10} alkenyl, C_{1-10} alkenoyl, C_{6-12} aryl, C_3 - C_{12} hetaryl having 1-3 heteroatoms selected from, S, N and O, C_{7-24} alkaryl, C_{7-24} aralkyl, substituted C_{1-10} alkyl, substituted C_{1-10} alkoxy, substituted C_6 - C_{14} aryl, substituted C_3 - C_{10} cycloalkyl having 0-3 heteroatoms selected from S, N and O, substituted C_{3-12} hetaryl having 1-3 heteroatoms selected from S, N and O, substituted C_{7-24} alkaryl or substituted C_7 - C_{24} aralkyl where R_z is a substituted group, it is substituted by halogen up to per halo, hydroxy, C_{1-10} alkyl, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{1-10} alkoxy, C_{6-12} aryl, C_{1-6} halo substituted alkyl up to per halo alkyl, C_6 - C_{12} halo substituted aryl up to per halo aryl, C_3 - C_{12} halo substituted cycloalkyl up to per halo cycloalkyl having 0-3 heteroatoms selected from N, S and O, halo substituted C_3 - C_{12} hetaryl up to per halo hetaryl having 1-3 heteroatoms selected from O, N and S, halo substituted C_7 - C_{24} aralkyl up to per halo aralkyl, halo substituted C_7 - C_{24} alkaryl up to per halo alkaryl, and $-C(O)R_g$,

R_a and R_b are,

a) independently hydrogen,

a carbon based moiety selected from the group consisting of C_1 - C_{10} alkyl, C_1 - C_{10} alkoxy, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{1-10} alkenoyl, C_{6-12} aryl, C_{3-12} hetaryl having 1-3 heteroatoms selected from O, N and S, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from N, S and O, C_{7-24} aralkyl, C_7 - C_{24} alkaryl, substituted C_{1-10} alkyl, substituted C_{1-10} alkoxy, substituted C_{3-10} cycloalkyl, having 0-3 heteroatoms selected from N, S and O, substituted C_{6-12} aryl, substituted C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, substituted C_{7-24} aralkyl, substituted C_{7-24} alkaryl, where R_a and R_b are a substituted group, they are substituted by halogen up to per halo, hydroxy, C_{1-10} alkyl, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{1-10} alkoxy, C_{6-12} aryl, C_{1-6} halo substituted alkyl up to per halo alkyl, C_6 - C_{12} halo substituted aryl up to per halo aryl, C_3 - C_{12} halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C_3 - C_{12} hetaryl up to per halo heteraryl, halo substituted C_7 -

C₂₄ aralkyl up to per halo aralkyl, halo substituted C₇-C₂₄ alkaryl up to per halo alkaryl, and -C(O)R_g; or

-OSi(R_f)₃ where R_f is hydrogen, C₁₋₁₀ alkyl, C₁₋₁₀ alkoxy, C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₆₋₁₂ aryl, C₃-C₁₂ hetaryl having 1-3 heteroatoms selected from O, S and N, C₇₋₂₄ aralkyl, substituted C₁₋₁₀ alkyl, substituted C₁-C₁₀ alkoxy, substituted C₃-C₁₂ cycloalkyl having 0-3 heteroatoms selected from O, S and N, substituted C₃-C₁₂ heteraryl having 1-3 heteroatoms selected from O, S, and N, substituted C₆₋₁₂ aryl, and substituted C₇₋₂₄ alkaryl, where R_f is a substituted group it is substituted halogen up to per halo, hydroxy, C₁₋₁₀ alkyl, C₃₋₁₂ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from N, S and O, C₁₋₁₀ alkoxy, C₆₋₁₂ aryl, C₇-C₂₄ alkaryl, C₇-C₂₄ aralkyl, C₁₋₆ halo substituted alkyl up to per halo alkyl, C₆-C₁₂ halo substituted aryl up to per halo aryl, C₃-C₁₂ halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C₃-C₁₂ hetaryl up to per halo heteraryl, halo substituted C₇-C₂₄ aralkyl up to per halo aralkyl, halo substituted C₇-C₂₄ alkaryl up to per halo alkaryl, and -C(O)R_g,

or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O with substituents selected from the group consisting of halogen up to per halo, hydroxy, C₁₋₁₀ alkyl, C₃₋₁₂ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from N, S and O, C₁₋₁₀ alkoxy, C₆₋₁₂ aryl, C₇-C₂₄ alkaryl, C₇-C₂₄ aralkyl, halo substituted C₁₋₆ alkyl up to per halo alkyl, halo substituted C₆-C₁₂ aryl up to per halo aryl, halo substituted C₃-C₁₂ cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C₃-C₁₂ hetaryl up to per halo heteraryl, halo substituted C₇-C₂₄ aralkyl up to per halo aralkyl, halo substituted C₇-C₂₄ alkaryl up to per halo alkaryl, and -C(O)R_g,

or

c) one of R_a or R_b is $-C(O)-$, a C_1-C_5 divalent alkylene group or a substituted C_1-C_5 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1-C_5 divalent alkylene group are selected from the group consisting of halogen, hydroxy, C_{1-10} alkyl, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{1-10} alkoxy, C_{6-12} aryl, C_7-C_{24} alkaryl, C_7-C_{24} aralkyl, C_{1-6} halo substituted alkyl up to per halo alkyl, C_6-C_{12} halo substituted aryl up to per halo aryl, C_3-C_{12} halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C_3-C_{12} hetaryl up to per halo heteraryl, halo substituted C_7-C_{24} aralkyl up to per halo aralkyl, halo substituted C_7-C_{24} alkaryl up to per halo alkaryl, and $-C(O)R_g$,

where R_g is C_{1-10} alkyl; $-CN$, $-CO_2R_d$, $-OR_d$, $-SR_d$, $-NO_2$, $-C(O)R_e$, $-NR_dR_e$, $-NR_dC(O)OR_e$ and $-NR_dC(O)R_e$, and R_d and R_e are independently selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{3-10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, C_{6-12} aryl, C_3-C_{12} hetaryl with 1-3 heteroatoms selected from O, N and S and C_7-C_{24} aralkyl, C_7-C_{24} alkaryl, up to per halo substituted C_1-C_{10} alkyl, up to per halo substituted C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, up to per halo substituted C_6-C_{14} aryl, up to per halo substituted C_3-C_{12} hetaryl having 1-3 heteroatoms selected from O, N, and S, halo substituted C_7-C_{24} alkaryl up to per halo alkaryl, and up to per halo substituted C_7-C_{24} aralkyl,

W is independently selected from the group consisting of $-CN$, $-CO_2R^7$, $-C(O)NR^7R^7$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, C_2-C_{10} alkenyl, C_1-C_{10} alkenoyl, C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_6-C_{14} aryl, C_7-C_{24} alkaryl, C_7-C_{24} aralkyl, C_3-C_{12} heteroaryl having 1-3 heteroatoms selected from O, N and S, C_4-C_{23} alkheteroaryl having 1-3 heteroatoms selected from O, N and S, substituted C_1-C_{10} alkyl, substituted C_1-C_{10} alkoxy, substituted C_2-C_{10} alkenyl, substituted C_1-C_{10} alkenoyl, substituted C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, substituted C_6-C_{12} aryl, substituted C_3-C_{12} hetaryl having 1-3 heteroatoms selected from O, N and

S, substituted C₇-C₂₄ aralkyl, substituted C₇-C₂₄ alkaryl, substituted C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S, and -Q-Ar;

R⁷ is independently selected from H, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₂-C₁₀ alkenyl, C₁-C₁₀ alkenoyl, C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₆-C₁₄ aryl, C₃-C₁₃ hetaryl having 1-3 heteroatoms selected from O, N and S, C₇-C₁₄ alkaryl, C₇-C₂₄ aralkyl, C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S, up to per-halosubstituted C₁-C₁₀ alkyl, up to per-halosubstituted C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, N and S, up to per-halosubstituted C₆-C₁₄ aryl, up to per-halosubstituted C₃-C₁₃ hetaryl having 1-3 heteroatoms selected from O, N and S, up to per-halosubstituted C₇-C₂₄ aralkyl, up to per-halosubstituted C₇-C₂₄ alkaryl, and up to per-halosubstituted C₄-C₂₃ alkheteroaryl; and

each Z is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₂-C₁₀ alkenyl, C₁-C₁₀ alkenoyl, C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, N and S, C₆-C₁₄ aryl, C₃-C₁₃ hetaryl having 1-3 heteroatoms selected from O, N and S, C₇-C₂₄ alkaryl, C₇-C₂₄ aralkyl, C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S, substituted C₁-C₁₀ alkyl, substituted C₁-C₁₀ alkoxy, substituted C₂-C₁₀ alkenyl, substituted C₁-C₁₀ alkenoyl, substituted C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, N and S, substituted C₆-C₁₂ aryl, substituted C₇-C₂₄ alkaryl, substituted C₇-C₂₄ aralkyl and substituted C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S; wherein if Z is a substituted group, the one or more substituents are selected from the group consisting of -CN, -CO₂R⁷, -COR⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NO₂, -NR⁷R⁷, -NR⁷C(O)R⁷, and -NR⁷C(O)OR⁷.

3. (Amended) A method [compound] as in claim 1 wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m-, -CHX^a-, -CX^a-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, X^a is halogen and R⁷ is as defined in claim 1.

6. (Amended) A method [compound] of claim 1 wherein B of Formula I is an unsubstituted phenyl group, an unsubstituted pyridyl group, an unsubstituted pyrimidinyl, a phenyl group substituted by a substituent selected from the group consisting of halogen and W_n wherein W and n are as defined in claim 1, a pyrimidinyl group substituted by a substituent selected from the group constituting of halogen and W_n, whereas W and n are as defined in Claim 1, or a substituted pyridyl group substituted by a substituent selected from the group consisting of halogen and W_n wherein W and n are as defined in claim 1.

7. (Amended) A method [compound] of claim 6 wherein B of Formula I is a substituted phenyl group, a substituted pyrimidinyl group, or substituted pyridyl group substituted 1 to 3 times by 1 or more substituents selected from the group consisting of -CN, halogen, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, -OH, up to per halo substituted C₁-C₁₀ alkyl, up to per halo substituted C₁-C₁₀ alkoxy or phenyl substituted by halogen up to per halo.

8. (Amended) A method [compound] of claim 1, wherein L, the six member cyclic structure bound directly to D, is a substituted or unsubstituted 6 member aryl moiety or a substituted or unsubstituted 6 member hetaryl moiety, wherein said hetaryl moiety has 1 to 4 members selected from the group of heteroatoms consisting of nitrogen, oxygen and sulfur with the balance of said hetaryl moiety being carbon, wherein the one or more substituents are selected from the group consisting of halogen and W_n wherein W and n are as defined in claim 1.

9. (Amended) A method [compound] of claim 8, wherein L, the 6 member cyclic structure bound directly to D, is a substituted phenyl, unsubstituted phenyl, substituted pyrimidinyl, unsubstituted pyrimidinyl, substituted pyridyl or unsubstituted pyridyl group.

10. (Amended) A method [compound] of claim 1, wherein said substituted cyclic moiety L¹ comprises a 5 to 6 membered aryl moiety or hetaryl moiety, wherein said heteraryl moiety comprises 1 to 4 members selected from the group of heteroatoms consisting of nitrogen, oxygen and sulfur.

11. (Amended) A method [compound] of claim 2, wherein said substituted cyclic moiety L¹ is phenyl, pyridinyl or pyrimidinyl.

12. (Amended) A method [compound] of claim 3, wherein said substituted cyclic moiety L¹ is phenyl, pyridinyl or pyrimidinyl.

13. (Amended) A method [compound] of claim 8, wherein said substituted cyclic moiety L¹ is phenyl, pyridinyl or pyrimidinyl.

15. (Amended) A method [compound] of claim 8, wherein said substituted cyclic moiety L¹ is phenyl, pyridinyl or pyrimidinyl.

17. (Amended) A method [compound] of claim 10, wherein said substituted cyclic moiety L¹ is phenyl, pyridinyl or pyrimidinyl.

18. (Amended) A method [compound] of claim 17 [12], wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m-CHX^a-, -CX₂^a-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, X^a is halogen and R⁷ is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.

19. (Amended) A method [compound] of claim 15, wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m-CHX^a-, -CX₂^a-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, X^a is halogen and R⁷ is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.

21. (Amended) A method [compound] of claim 17, wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m-CHX^a-, -CX₂^a-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, X^a is halogen and R⁷ is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.

27. (Amended) A method [compound] of claim 21 wherein L^1 is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C_1 - C_{10} alkyl, up to per halo substituted C_1 - C_{10} alkyl, -CN, -OH, halogen, C_1 - C_{10} alkoxy and up to per halo substituted C_1 - C_{10} alkoxy.

28. (Amended) A method [compound] of claim 1 wherein L^1 is substituted by - $C(O)R_x$.

32. (Amended) A method [compound] of claim 1 wherein L^1 is substituted by - $C(O)R_x$ or $-SO_2R_x$, wherein R_x is NR_aR_b .

33. (Amended) A method [compound] of claim 13 wherein L^1 is substituted by - $C(O)R_x$ or $-SO_2R_x$, wherein R_x is NR_aR_b , and R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

$-OSi(R_f)_3$ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_a or R_b is $-C(O)-$, a C_1-C_5 divalent alkylene group or a substituted C_1-C_5 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1-C_5 divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.

37. (Amended) A method [compound] of claim 21 wherein L^1 is substituted by $-C(O)R_x$ or $-SO_2R_x$, wherein R_x is NR_aR_b and R_a and R_b are independently hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.

38. (Amended) A method for the treatment of cancerous cell growth mediated by RAF kinase, comprising administering a compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is $-NH-C(O)-NH-$,

A is a substituted moiety of up to 40 carbon atoms of the formula: $-L-(M-L^1)_q$, where L is a 6 membered aryl moiety or a 6 membered hetaryl moiety bound directly to D, L^1 comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and L^1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur,

wherein L^1 is substituted by at least one substituent selected from the group consisting of $-SO_2R_x$, $-C(O)R_x$ and $-C(NR_y)R_z$,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo,

R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

$-OSi(R_f)_3$ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_a or R_b is $-C(O)-$, a C_1-C_5 divalent alkylene group or a substituted C_1-C_5 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1-C_5 divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L¹ is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and W_n, where n is 0-3;

wherein each W is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)NR⁷R⁷, -C(O)-R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, -Q-Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NR⁷R⁷, -NO₂, -NR⁷C(O)R⁷, -NR⁷C(O)OR⁷ and halogen up to per-halo; with each R⁷ independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m- CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, and X^a is halogen;

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents are selected from the group consisting of -CN, -CO₂R⁷, -COR⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NO₂, -NR⁷R⁷, -NR⁷C(O)R⁷, and -NR⁷C(O)OR⁷, with R⁷ as defined above; and

wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m- CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, X^a is halogen.

39. (Amended) A method for the treatment of cancerous cell growth mediated by RAF kinase, comprising administering a compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH- ,

A is a substituted moiety of up to 40 carbon atoms of the formula: $\text{-L-(M-L}^1\text{)}_q$, where L is a substituted or unsubstituted phenyl or [peritoneal] pyridinyl moiety bound directly to D, L^1 comprises a substituted phenyl, [peritoneal] pyridinyl or [pyrimidinyl] pyrimidinyl moiety, M is a bridging group having at least one atom, q is an integer of from 1-3; and

B is a substituted or unsubstituted phenyl or pyridine group bound directly to D,

wherein L^1 is substituted by at least one substituent selected from the group consisting of $\text{-SO}_2\text{R}_x$, -C(O)R_x and $\text{-C(NR}_y\text{)R}_z$,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo, and ;

R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

$\text{-OSi(R}_f\text{)}_3$ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms

selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_a or R_b is $-C(O)-$, a C_1-C_5 divalent alkylene group or a substituted C_1-C_5 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1-C_5 divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L^1 is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and W_n , where n is 0-3;

wherein each W is independently selected from the group consisting of $-CN$, $-CO_2R^7$, $-C(O)NR^7R^7$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, $-Q-Ar$, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of $-CN$, $-CO_2R^7$, $-C(O)R^7$, $-C(O)NR^7R^7$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NO_2$, $-NR^7C(O)R^7$, $-NR^7C(O)OR^7$ and halogen up to per-halo; with each R^7 independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is $-O-$, $-S-$, $-N(R^7)-$, $-(CH_2)_m-$, $-C(O)-$, $-CH(OH)-$, $-(CH_2)_mO-$, $-(CH_2)_mS-$, $-(CH_2)_mN(R^7)-$, $-O(CH_2)_m-$, $-CHX^a-$, $-CX^a_2-$, $-S-(CH_2)_m-$ and $-N(R^7)(CH_2)_m-$, where $m=1-3$, and X^a is halogen;

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1} , wherein $n1$ is 0 to 3 and each Z is independently selected from the group consisting of $-CN$, $-CO_2R^7$, $-C(O)R^7$, $-C(O)NR^7R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one

or more substituents selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^7$, $-\text{COR}^7$, $-\text{C}(\text{O})\text{NR}^7\text{R}^7$, $-\text{OR}^7$, $-\text{SR}^7$, $-\text{NO}_2$, $-\text{NR}^7\text{R}^7$, $-\text{NR}^7\text{C}(\text{O})\text{R}^7$, and $-\text{NR}^7\text{C}(\text{O})\text{OR}^7$; and

wherein M is one or more bridging groups selected from the group consisting of $-\text{O}-$, $-\text{S}-$, $-\text{N}(\text{R}^7)-$, $-(\text{CH}_2)_m-$, $-\text{C}(\text{O})-$, $-\text{CH}(\text{OH})-$, $-(\text{CH}_2)_m\text{O}-$, $-(\text{CH}_2)_m\text{S}-$, $-(\text{CH}_2)_m\text{N}(\text{R}^7)-$, $-\text{O}(\text{CH}_2)_m-\text{CHX}^a-$, $-\text{CX}^a_2-$, $-\text{S}-(\text{CH}_2)_m-$ and $-\text{N}(\text{R}^7)(\text{CH}_2)_m-$, where $m=1-3$, X^a is halogen.

44. (Amended) A method [compound] as in claim 38 wherein substituents for B and L and additional substituents for L^1 , are selected from the group consisting of $\text{C}_1\text{-C}_{10}$ alkyl up to per halo substituted $\text{C}_1\text{-C}_{10}$ alkyl, CN, OH, halogen, $\text{C}_1\text{-C}_{10}$ alkoxy and up to per halo substituted $\text{C}_1\text{-C}_{10}$ alkoxy.

45. (Amended) A method [compound] as in claim 39 wherein substituents for B and L and additional substituents for L^1 , are selected from the group consisting of $\text{C}_1\text{-C}_{10}$ alkyl up to per halo substituted $\text{C}_1\text{-C}_{10}$ alkyl, CN, OH, halogen, $\text{C}_1\text{-C}_{10}$ alkoxy and up to per halo substituted $\text{C}_1\text{-C}_{10}$ alkoxy.

46. (Amended) A method [compound] of claim 38 wherein L^1 is substituted by $\text{C}(\text{O})\text{R}_x$ or SO_2R_x .

47. (Amended) A method [compound] of claim 39 wherein L^1 is substituted by $\text{C}(\text{O})\text{R}_x$ or SO_2R_x .

48. (Amended) A method [compound] of claim 46 wherein R_x is NR_aR_b and R_a and R_b are independently hydrogen and a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen..

49. (Amended) A method [compound] of claim 47 wherein R_x is NR_aR_b and R_a and R_b are independently hydrogen and a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.

50. (Amended) A method [compound] of claim 1 wherein the compound of formula 1 [which] is a pharmaceutically acceptable salt [of a compound of formula I] selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

52. (Amended) A method [compound] of claim 33 wherein the compound of formula 1 [which] is a pharmaceutically acceptable salt [of a compound of formula 1] selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

53. (Amended) A method [compound] of claim 38 [which] wherein the compound formula 1 is a pharmaceutically acceptable salt [of a compound of formula I] selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

54. (Amended) A method [compound] of claim 39 [which] wherein the compound of formula 1 is a pharmaceutically acceptable salt [of a compound of formula I] selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.